REMARKS

Claims 1-47 are pending. Claim 41 has been withdrawn from consideration. Claims 1 to 40 and 42 to 47 stand variously rejected under 35 U.S.C. § 112, first and second paragraphs. In view of the following remarks and foregoing amendments, Applicants respectfully request reconsideration of the application.

Overview of the Amendments

Claims 4, 5, 8, 22, 25, 29 and 42 have been amended to correct antecedent basis. Claim 36 has been amended to correct a typographical error. Claims 22 and 25 have been amended to specify that the claimed composition includes a pharmaceutically acceptable vehicle, for example as described on page 26, lines 4 to 8 and page 66, lines 20 to 26 of the specification. Claim 21 has been amended to specify that the cell is a tumor cell. Further, claim 43 has been amended to clarify that the polypeptide is derived from HIV, as described for example, on page 23, lines 1 to 8 of the specification.

New claims 67-77 have been added. These new claims find support throughout the specification and claims as originally filed. Furthermore, Applicants note that the Office has indicated that the new claims are fully enabled by the specification as filed. (See, Office Action, page 6).

The amendments are made to expedite prosecution and are not made for reasons related to patentability. No new matter has been added as a result of these amendments and entry thereof is respectfully requested.

Information Disclosure Statement

The Examiner has objected to the IDS filed October 24, 2000 because it did not properly cite one of the journal articles listed on the 1449. Submitted herewith is a supplemental IDS including the correct citation of this article. Applicants respectfully request that the Examiner initial the new 1449 form.

Restriction Requirement

Applicants acknowledge with appreciation the withdrawal of the restriction as between groups I-VI as well as withdrawal of the election of species requirement. Thus, Claims 1-40 and 42-47 (Group I) are pending and have been examined. Applicants expressly reserve their right under 35 USC §121 to file one or more divisional applications directed to the nonelected subject matter during the pendency of this application.

Claim Objections

Claim 36 is objected to for having a typographical error. By amendment herein, the error has been corrected, thereby obviating this objection.

35 U.S.C. 112, First Paragraph, Written Description

Claim 4 stands rejected as allegedly not described by the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the invention at the time of filing. (Office Action, page 4). In support of this rejection, the Examiner alleges that the specification does not provide sufficient guidance for production of an expression cassette comprising a polynucleotide sequence encoding an HIV Pol polypeptide and one or more nucleic acids encoding one or more cytokines. (Office Action, page 5). In sum, it is maintained that the specification as filed is not sufficient to support the invention of claim 4.

Applicants traverse the rejection and the supporting remarks.

Determining whether the written description requirement is satisfied is a question of fact. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *Regents of University of California v. Eli Lilly* 43 USPQ2d 1398 (Fed. Cir. 1997). The burden is on the Examiner to provide evidence as to why a skilled artisan would <u>not</u> have recognized that the applicant was in possession of claimed invention at the time of filing. Further, such a determination requires reading the disclosure in light of the knowledge possessed by those skilled in the art including affidavits by experts regarding what the specification reasonably conveys to the skilled artisan. *In re Alton,* 37 USPQ2d 1578 (Fed. Cir. 1996). Thus, an applicant need only show that the parent disclosure conveys to

one of skill in the art that they were in possession of the claimed invention at the time of filing. *In re Wertheim,* 191 USPQ 90 (CCPA 1976).

The specification as filed fully satisfies these written description requirements. In fact, as noted by the Examiner, claim 4 is directed to expression constructs comprising a polynucleotide sequence encoding an HIV Pol polypeptide and one or more nucleic acids encoding one or more cytokines. The specification discloses, for example on pages 37 and 49-51 multiple examples of suitable cytokines and nucleic acids encoding these cytokines. Thus, as described throughout the specification, one of skill in the art could readily design and use the constructs of claim 4 in light of the teachings of the specification and level of knowledge in the art. The specification provides detailed guidance on how to construct expression vectors generally (See, *e.g.,* Section 2.2.3 of the specification); the type of cytokines that may be used in these expression vectors (See, *e.g.,* Section 2.2.1.5 starting on page 37 of the specification) and sequences encoding these cytokines (See, *e.g.,* Section 2.3.2 staring on page 49 of the specification). The specification references numerous patent and other publications which describe sequences encoding cytokines and expression constructs carrying these sequences. Indeed, these sequences were publically available at the time of filing, either by purchase or on public databases such as GenBank. In light of the extensive teachings of the specification and the knowledge of those skilled in the art regarding cytokines (and sequences encoding these cytokines), it is plain that the specification reasonably conveys to a skilled artisan that the inventors had invented an expression construct encoding an HIV Pol polypeptide and one or more cytokines. Accordingly, the written description requirement is satisfied and the rejection should be withdrawn.

Further evidence is presented herewith in the form of a Rule 132 Declaration by Dr. Susan Wilson. In particular, Dr. Wilson states:

> 6. When the specification was filed, it clearly conveyed to a typical scientist that the inventors had in their possession the invention of claim 4 (as set forth in paragraph 4, above). By "in their possession," I mean that the inventors contemplated the expression cassette as set forth in claim 4 and that they had, using the specification and information available to a typical scientist, a practical way of making such an expression cassette. Thus, I believe that a typical scientist would have understood the

specification clearly described all of the various aspects of claim 4. I base this belief on the facts set forth below.

7. First, at the time the specification was filed, it was widely known how to construct expression cassettes, including expression vectors having two or more polypeptide-encoding sequences. Such methods are described in detail in the specification, for example, in Section 2.2.3 of the specification. Therefore, it is my opinion that construction of an expression cassette as set forth in claim 4 would have been routine to a typical scientist working in this area in view of the teachings of the specification.

8. Second, it would have been clear to a typical scientist that the inventors had in their possession the various polynucleotide components of the expression cassette of claim 4. HIV *Pol*-encoding sequences (SEQ ID NOs:30, 31 and 32) were clearly set forth in the Figures 8, 9 and 10 at the time of filing. Additionally, the specification clearly describes how to determine those sequences having 90% sequence identity to the claimed HIV *Pol*-encoding sequences of SEQ ID NOs:30, 31 and 32. (See, for example page 19, line 19 to page 22, which describes the use of available programs for calculating identity or similarity between sequences). Details and examples of how to determine sequence identity are also provided. (See, e.g., page 20, lines 1-7 and 14-25 and page 75, lines 29-33). Thus, it is my opinion that the HIV *Pol*-encoding sequences of the expression cassette of claim 4 are fully described in the specification.

9. Third, at the time the specification was filed, it would have been clear to a typical scientist that the inventors' specification fully described and contemplated an expression cassette that included both HIV *Pol*-encoding polypeptides as set forth above in paragraph 5 and one or more additional cytokine-encoding polynucleotides. Both cytokines themselves and polynucleotides encoding these cytokines were widely known at the time of filing and were disclosed in the specification as filed. (See, *e.g.*, Section 2.2.1.5 starting on page 37 of the specification; and Section 2.3.2 staring on page 49 of the specification). Such cytokines were also commercially or publically available, as were polynucleotide sequences encoding these cytokines. (See, *e.g.*, page 37, lines 21-29 of the specification). Taken as whole, the specification unambiguously conveyed to a typical scientist that the inventors contemplated including a polynucleotide encoding one or more cytokines in expression cassettes comprising the HIV *Pol*-encoding sequences disclosed in the specification. In sum, based on the disclosure of the specification and the level of knowledge of a typical scientist regarding cytokines and expression cassettes at the time of filing, I believe that the specification as filed clearly conveys that the applicants had invented the expression cassettes as set forth in claim 4. (See, Wilson Declaration, attached hereto).

In sum, the evidence of record, including the attached declaration establish that the written description rejection of claim 4 is improper and should be withdrawn.

35 U.S.C. 112, First Paragraph, Enablement

Claims 1-40 and 42-47 stand rejected under 35 U.S.C. 112, first paragraph as allegedly not enabled by the specification as filed. In particular, it is alleged that while the specification is enabling for (1) an expression cassette comprising a polynucleotide sequence encoding a Pol polypeptide as set forth in SEQ ID NO:30, 31 or 32; (2) the expression cassette of (1) further comprising a sequence encoding a viral polypeptide selected from Gag, Env, vif, vpr, tat, rev, vpu, nef, and combinations thereof; (3) a composition for generating an immune response in a mammal comprising the expression cassette of (1); (7) a method for generating an immune response in a mammal comprising intramuscularly administering the expression cassette of (1) to a mammal, it is does not enable the rest of the claims. (Office Action, page 6). The Examiner also cites several references in support of the enablement rejection, alleging that the state of the art in vaccines is unpredictable. (Office Action, pages 7-8). Additionally, it is alleged that it would require undue experimentation to make and/or use sequences having at least 90% identity to those presented as SEQ ID NOs:30-32. (Office Action, page 10).

Applicants traverse the rejections and supporting remarks.

Before addressing each issue raised by the Office, Applicants note the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Whenever the PTO makes a rejection for failure to teach how to make and/or use the invention, the PTO must explain its reasons for the rejection and support the rejection with (i) acceptable evidence, or (ii) reasoning which contradicts the Applicants' claim: the reasoning must be supported by current literature as a whole and the PTO must prove the disclosure requires undue experimentation. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971). For the reasons detailed below, the Office has failed to establish a *prima facie* case of non-enablement with respect to any of the pending claims.

Immunogenic Compositions and Methods of Inducing an Immune Response

Applicants also note that is well-settled that the enablement requirement is satisfied if the applicant's specification teaches one of skill in the art how to make and use the claimed invention without undue experimentation. *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988). Further the "invention" referred to in the enablement requirement of section 112 is the claimed invention." *See, Christianson v. Colt Industries Operating Corp.* 3 USPQ2d 1241 (Fed. Cir. 1987), emphasis added. Thus, the Office must first determine what each claim recites when the claim is considered as a whole, not when its parts are analyzed individually. See, Training Manual on Enablement, page 9. Moreover, the existence of inoperative or ineffective embodiments does not mean that the enablement requirement if not satisfied. Indeed, if any use of multiple uses disclosed in the specification are enabled, the application is enabling. See, Training Manual, page 21.

In the pending case, the Office acknowledges that the claims are enabled for specific sequences and use of these sequences to generate immunological responses in mammals when administered intramuscularly. (Office Action, page 5). However, in support of the enablement rejection, the Examiner cites numerous references allegedly showing the unpredictability of nucleic acid vaccines, particular in the filed of HIV (citing Gurunathan, Anderson, Verma, Nathanson, Prince, Azevedo and McCluskie). (Office Action, pages 6-13). It is also alleged that the disclose does not enable the use of cells *in vitro*, *in vivo* and *ex vivo.* (Office Action, page 11).

As a threshold matter, Applicants note that only 22-47 are directed to compositions and methods for generating an immune response and none of these claims recite "vaccine compositions" or "methods of treating (or vaccinating against) HIV." Rather, they are drawn to compositions comprising particular polynucleotide sequences or to methods of generating an immunological response in a mammal using these compositions. As is well-known and described, for example, on page 15, the generation of an immunological response does not necessarily provide protection and/or therapy. Therefore, when properly interpreted in light of the specification, the pending claims are directed to methods of eliciting an immune responses and the enablement requirement is satisfied by Applicants' showing that these methods elicit immune responses. (See, Examples).

Furthermore, Applicants submit that the Office cannot reject the claims on the basis that one "implied" use may be ineffective or inoperative. In other words, the fact that the enabled cellular and humoral immune responses may or may not be protective and/or therapeutic against HIV is not relevant to the enablement inquiry in this case. As noted above, all that is required to satisfy enablement is that specification enable one use. *See, e.g., In re Angstadt,* 190 USPQ 214 (CCPA 1976). In the case at hand, there is no dispute that Applicants have enabled methods of eliciting an immunological response in a subject using an expression cassette as claimed. (See, attached Exhibit A) Thus, Applicants have plainly shown how to make and use the claimed invention and Applicants are not required to establish whether these immunological responses are protective or therapeutic. In sum, Applicants' specification fully enables the pending claims by enabling not only a single use, but by enabling the claims throughout their scope.

Despite the failure of the Office to make a case for non-enablement, Applicants address why the claims are enabled throughout their scope. As previously discussed, enablement is fact-dependent. An applicant does not need to specify the dosage or method of use if it is known to one of skill in the art that such information could be readily obtained. *See, e.g.*, USPTO Training Materials on Enablement, page 20. In fact, a considerable amount of routine experimentation is permissible if the specification provides a reasonable amount of guidance, with respect to the direction in which experimentation should proceed, to enable the determination of how to practice a desired embodiment of the claimed invention. *Ex parte Forman, supra*; *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Further, the standards articulated in *In re Wands* can be used to help determine whether the specification at issue is in fact enabling. Indeed, the situation in *Wands* is highly analogous to that at hand. In *Wands,* the Federal Circuit held that claims to generic monoclonal antibodies were enabled by a specification that taught the entire procedure of making monoclonal antibodies. Moreover, in view of the high level of skill in the art and routine nature of each step of the antibody-making procedure, the court held that the amount of experimentation required to make other monoclonals was extensive, but not undue.

Similarly, in the pending case, Applicants submit that their specification clearly sets forth the procedure for determining routes of administration of expression cassettes as well as dosages and delivery regimes. Applicants direct the Examiner's attention to Examples 4-7 and the attached Exhibit A that demonstrates the claimed expression constructs induce an immune response in a mammal when made, administered and tested for immunogenicity following the teachings of the specification. (See, for example, Section 2.4 of the specification, pages 57 to 71, regarding administration; page 80-81 for assessing immunogenic responses; and Examples 4-7). Thus, Applicants have rebutted any allegation that the specification does not fully enable the claims and that there is more than sufficient guidance as to the claimed methods in the specification.

The References Do Not Establish Unpredictability

Applicants also traverse the Examiner's assertion that the gene therapy references establish that the claimed invention is unpredictable. (Gurunathan, Verma Anderson, Prince, Nathanson, Azevedo cited on pages 6-13 of the Office Action). These references do no such thing. None of these reference address using the particularly claimed expression cassettes to generate an immune response. Gurunathan is directed to the use of CD40LT as an adjuvant. Anderson is directed a gene-therapy in the context of treatment regimes. Similarly, Verma is directed to issues involved in "alleviating the symptoms of disease" (See, Abstract). Nathanson, Prince and McCluskie are also exclusively directed to vaccines and therapy. For its part, Azevedo is a general review of plasmid-based DNA immunization and clearly teaches that these vectors are known to generate an immune response. (See, "concluding remarks). Azevedo goes to state that the particular nature of the immune response generated can be readily tested for each antigen. (See, "concluding remarks"). Thus, these references are a far cry away from establishing that methods of eliciting an immune response to the claimed expression cassettes are not enabled by Applicants' specification. In fact, Applicants' specification describes and demonstrates the generation of an immune response and, accordingly, the various references cited by the Office are not relevant to the claimed invention and certainly do not establish unpredictability of the claimed invention.

Percent Identity

The Examiner also asserts that the specification does not provide sufficient description for one of skill in the art to make and/or use a sequence having "90% identity" to the sequences of SEQ ID NO:30 to 32. Applicants disagree with the Examiner's assessment of the level of enabling disclosure in the present applicant in regard to "percent identity." The use of available programs for calculating identity or similarity between sequences is fully disclosed in the specification, for example at page 19, line 19 to page 22. Exemplary default parameters for these available programs are set forth, on page 20, lines 1-7 and 14-25. These programs and parameters were also used and are exemplified at page 75, lines 29-33. Indeed, the use of such default parameters is routine and well within the abilities of one having ordinary skill in the art -- this is the manner in which the Patent Office searches the database for sequences that may correspond to the claimed sequences.

In sum, when evidence of record is examined, Applicants submit that it is plain that it would not require undue experimentation to practice the claimed invention, given the guidance found in the specification and state of the art. The claimed invention is, therefore, fully enabled by the specification and Applicants respectfully request the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

35 U.S.C. 112, Second Paragraph

Claims 5, 8, 21, 22, 25, 29, 43 and 47 stand rejected under 35 U.S.C. 112, second paragraph as allegedly indefinite. Applicants address each rejection in turn below.

Claims 5, 8, 22, 25 and 42 are alleged to be indefinite for failing to have proper antecedent basis. Applicants have amended the claims herein to provide the requested language, thereby obviating this rejection.

Claims 22 and 25 are alleged to be indefinite due to the recitation of the phrase "comprising the expression cassette of claim ..." (Office Action, page 17). In particular, it is alleged that the transitional phrase comprising implies that there has to an additional element and the claims only set forth the element of the expression cassette. Applicants

Claim 29 is alleged to be indefinite due to the use of the term "an" when referring to the a composition described in another claim. Thus, claim 29 has been amended herein to have proper antecedent basis.

Claim 21 is alleged to be indefinite for reciting "tumor-derived." (Office Action, page 18). Because one of skill the art would understand the metes and bounds of this term, Applicants traverse. Nonetheless, in order to advance prosecution, the claim has been rewritten herein to obviate the rejection.

Claim 43 is alleged to be indefinite in the recitation of "HIV-derived." Because one of skill the art would understand the metes and bounds of this term, Applicants traverse. For example, on page 23, lines 1-8, Applicants set forth what it means for a polypeptide to be derived from another or for one viral polypeptide to be derived from another. Nonetheless, in order to advance prosecution, the claim has been rewritten herein to obviate the rejection.

Claim 47 is alleged to be indefinite in the recitation of "derived." Applicants direct the Examiner's attention to page 23, lines 4-8 of the specification, which clearly defined "derived from" in reference to viral polypeptides. Accordingly, Applicants submit that the claim is definite in the light of the teachings of the specification. By virtue of its dependency on claim 41, Applicants note that this claim is properly directed to a composition comprising (i) the expression cassette of claim 1 and (ii) a Gag polypeptide. Thus, the claim is not incomplete as written.

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicants submit that the boundaries of the pending claims are capable of being understood by one of ordinary skill in the art. Therefore, withdrawal of the rejections of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

III. CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

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Version Showing Changes Made to Claims

4. (Amended) The expression cassette of claim 1, further comprising one or more nucleic acids encoding one or more [viral] cytokines.

5. (Amended) A recombinant expression system for use in a selected host cell, comprising, [an] the expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected host cell.

8. (Amended) A cell comprising [an] the expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected cell.

21. (Amended) The cell of claim 8, wherein the cell is a tumor[-derived] cell.

22. (Amended) A composition for generating an immunological response, comprising [an] the expression cassette of claim 1.

25. (Amended) A composition for generating an immunological response, comprising [an] the expression cassette of claim 2.

29. (Amended) A method of immunization of a subject, comprising,
introducing [a] the composition of claim 22 into said subject under conditions that are compatible with expression of said expression cassette in said subject.

36. (Amended) The method of claim 30, wherein said composition is delivered using a particulate carrier.

42. (Amended) A method of generating an immune response in a subject, comprising
introducing into cells of said subject [an] the expression cassette of claim 1, under conditions that permit the expression of said polynucleotide and production of said polypeptide, thereby eliciting an immunological response to said polypeptide.

43. (Amended) The method of claim 42, where the method further comprises administration of [an HIV-derived] a polypeptide derived from an HIV.

Currently Pending Claim Set

1. An expression cassette, comprising
a polynucleotide sequence encoding a polypeptide including an HIV *Pol* polypeptide, wherein the polynucleotide sequence encoding said *Pol* polypeptide comprises a sequence having at least 90% sequence identity to the sequence presented of Figure 8 (SEQ ID NO:30); Figure 9 (SEQ ID NO:31) or Figure 10 (SEQ ID NO:32).

2. The expression cassette of claim 1, further comprising one or more nucleic acids encoding one or more viral polypeptides or antigens.

3. The expression cassette of claim 2, wherein the viral polypeptide or antigen is selected from the group consisting of Gag, Env, vif, vpr, tat, rev, vpu, nef and combinations thereof.

4. (Amended) The expression cassette of claim 1, further comprising one or more nucleic acids encoding one or more cytokines.

5. (Amended) A recombinant expression system for use in a selected host cell, comprising, the expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected host cell.

6. The recombinant expression system of claim 5, wherein said control elements are selected from the group consisting of a transcription promoter, a transcription enhancer element, a transcription termination signal, polyadenylation sequences, sequences for optimization of initiation of translation, and translation termination sequences.

7. The recombinant expression system of claim 5, wherein said transcription promoter is selected from the group consisting of CMV, CMV+intron A, SV40, RSV, HIV-Ltr, MMLV-ltr, and metallothionein.

8. (Amended) A cell comprising the expression cassette of claim 1, and wherein said polynucleotide sequence is operably linked to control elements compatible with expression in the selected cell.

9. The cell of claim 8, wherein the cell is a mammalian cell.

10. The cell of claim 9, wherein the cell is selected from the group consisting of BHK, VERO, HT1080, 293, RD, COS-7, and CHO cells.

11. The cell of claim 10, wherein said cell is a CHO cell.

12. The cell of claim 8, wherein the cell is an insect cell.

13. The cell of claim 12, wherein the cell is either *Trichoplusia ni* (Tn5) or Sf9 insect cells.

14. The cell of claim 8, wherein the cell is a bacterial cell.

15. The cell of claim 8, wherein the cell is a yeast cell.

16. The cell of claim 8, wherein the cell is a plant cell.

17. The cell of claim 8, wherein the cell is an antigen presenting cell.

18. The cell of claim 17, wherein the antigen presenting cell is a lymphoid cell selected from the group consisting of macrophage, monocytes, dendritic cells, B-cells, T-cells, stem cells, and progenitor cells thereof.

19. The cell of claim 8, wherein the cell is a primary cell.

20. The cell of claim 8, wherein the cell is an immortalized cell.

21. (Amended) The cell of claim 8, wherein the cell is a tumor cell.

22. (Amended) A composition for generating an immunological response, comprising the expression cassette of claim 1.

23. The composition of claim 22, further comprising one or more *Pol* polypeptides.

24. The composition of claim 23, further comprising an adjuvant.

25. (Amended) A composition for generating an immunological response, comprising the expression cassette of claim 2.

26. The composition of claim 25, further comprising a *Pol* polypeptide.

27. The composition of claim 26, further comprising one or more polypeptides encoded by the nucleic acid molecules of claim 2.

28. The composition of claim 27, further comprising an adjuvant.

29. (Amended) A method of immunization of a subject, comprising,
introducing the composition of claim 22 into said subject under conditions that are compatible with expression of said expression cassette in said subject.

30. The method of claim 29, wherein said expression cassette is introduced using a gene delivery vector.

31. The method of claim 30, wherein the gene delivery vector is a non-viral vector.

32. The method of claim 30, wherein said gene delivery vector is a viral vector.

33. The method of claim 32, wherein said gene delivery vector is a Sindbis-virus derived vector.

34. The method of claim 32, wherein said gene delivery vector is a retroviral vector.

35. The method of claim 32, wherein said gene delivery vector is a lentiviral vector.

36. (Amended) The method of claim 30, wherein said composition is delivered using a particulate carrier.

37. The method of claim 30, wherein said composition is coated on a gold or tungsten particle and said coated particle is delivered to said subject using a gene gun.

38. The method of claim 30, wherein said composition is encapsulated in a liposome preparation.

39. The method of any of claims 30-38, wherein said subject is a mammal.

40. The method of claim 39, wherein said mammal is a human.

41. Withdrawn.

42. (Amended) A method of generating an immune response in a subject, comprising

introducing into cells of said subject the expression cassette of claim 1, under conditions that permit the expression of said polynucleotide and production of said polypeptide, thereby eliciting an immunological response to said polypeptide.

43. (Amended) The method of claim 42, where the method further comprises administration of a polypeptide derived from an HIV.

44. The method of claim 43, wherein administration of the polypeptide to the subject is carried out before introducing said expression cassette.

45. The method of claim 43, wherein administration of the polypeptide to the subject is carried out concurrently with introducing said expression cassette.

46. The method of claim 43, wherein administration of the polypeptide to the subject is carried out after introducing said expression cassette.

47. The expression cassette of claim 2, wherein the viral polypeptide or antigen is selected from the group consisting of polypeptides derived from hepatitis B, hepatitis C and combinations thereof.

48. (New) An expression cassette comprising the polynucleotide sequence of SEQ ID NO:30, SEQ ID NO:31 or SEQ ID NO:32.

49. (New) The expression cassette of claim 48 further comprising a nucleotide sequence encoding a viral polypeptide selected from the group consisting of Gag, Env, vif, vpr, tat, rev, vpu, nef and combinations thereof.

50. (New) A composition for generating an immunological response in a mammal comprising the expression cassette of claim 48.

51. (New) A method of generating an immune response in a mammal, the method comprising the step of intramuscularly administering the expression cassette of claim 48 to said mammal.